NATIONAL MARROW DONOR PROGRAM®

Entrusted to operate the C.W. Bill Young Cell Transplantation Program,
including Be The Match Registry℠

August 14, 2009

Cdr. Elizabeth Montcalm-Smith
Office of Naval Research (ONR 342)
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-08-1-0058 between the Office of Naval Research and the National Marrow Donor Program

Dear Cdr. Montcalm-Smith:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of April 1, 2009 to June 30, 2009.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

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1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-08-1-0058

QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
APRIL 01, 2008 to JUNE 30, 2008
Period 6

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
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IIA. Contingency Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1 Aim 1: Secure Interest of Transplant Physicians	**Period 6 Activity:** • Held the 2009 RITN conference "Nuclear Terrorism: Hematology/Oncology Center Preparedness" in Bethesda, MD on May 18th (additional details of this conference are listed under Aim II.A 2.1).
IIA.1 Aim 2: GCSF in Radiation Exposure	**Period 6 Activity:** • No activity this period
IIA.1 Aim 3: Patient Assessment Guidelines and System Enhancements	**Period 6 Activity:** • Continued development of the Donor Contingency Portal project to improve response processes for selectively identified donors and to enhance the donor management teams' ability to monitor them.
IIA 1 Aim 4: National Data Collection Model	**Period 6 Activity:** • No activity this period
IIA. Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
IIA.2 Aim 1: Contingency Response Network	**Period 6 Activity:** • Conducted the 2009 RITN conference "Nuclear Terrorism: Hematology/Oncology Center Preparedness" in Bethesda, MD on May 18, 2009. o Ninety-two experts in their fields attended this conference. o Key note speaker was RADM Anne Kneble (Deputy Director for Preparedness Planning in the Office of the Assistant Secretary for Preparedness and Response, United States Department of Health and Human Services)

- Morning group sessions included:
  - Threat scenario overview
  - National Disaster Medical System
  - Medical response expectations 10, 100, 1000 miles from epicenter
  - Altered standards of medical care overview
  - NMDP planning and data collection
- Afternoon interactive breakout workgroups included (each session was held three times so attendees could attend all sessions):
  - Altered standards of care
  - Logistical issues – bed mgmt, use of non-hospital location, & staffing issues
  - Provision of medical care – early and late care
- The conference culminated with a report of findings by the afternoon session moderators

- **Meetings**:
  - Conducted three (3) monthly conference calls with RITN centers to assist in completion of required tasks and to improve integration into the network.
  - Distributed three (3) “Rad in the News” open source news summary reports to RITN centers and partner organizations with the intent to maintain awareness of international activities related to radioactive materials.
  - Held the RITN Steering Committee meeting on May 19, 2009 following the RITN educational conference. Meeting agenda included:
    - 2009 conference review
    - Update on tabletop Lessons Learned project
    - Coordination with HHS on triage of incident victims

	▪ Update on RITN-VA mapping project ▪ Update on JCHO interaction ▪ BARDA Presentation ▪ Tour of HHS Secretary's Emergency Operations Center
IIA.2 Aim 2: Sibling Typing Standard Operating Procedures	**Period 6 Activity:** • No activity this period
IIA. Contingency Preparedness – Hypothesis 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3 Aim 1: I.T. Disaster Recovery	**Period 6 Activity:** • Additional hardware and software was purchased, installed and configured to support disaster recovery testing. Additional network segments were also added to support the disaster recovery environment for completing this set of tests. • Completed the Disaster Recovery Testing for all Tier 1 applications in April 2009. In addition, the Disaster Recovery Smoke Test for Tier 2 through Tier 4 applications was completed in May 2009 and full Disaster Recovery testing for Tier 2 through 4 applications was successfully completed in June 2009.
IIA.3 Aim 2: Critical Facility and Staff Related Functions	**Period 6 Activity:** • **Business Continuity Planning:** o A variety of communication exercises were conducted by the NMDP to validate current procedures: ▪ A test of the Coordinating Center public address system from both the receptionist desk as well as from another work area within the Coordinating Center. ▪ A satellite telephone test to ensure RITN partners were familiar with the new Iridium satellite

telephones and to validate accountability.

- A mass emergency notification telephonic system test (recorded voice and TTY) to notify NMDP staff and Network Centers of incidents impacting NMDP operations and validate emergency contact phone numbers.
- Government Emergency Telecommunications Service (GETS) calling cards were tested to validate the ability of RITN centers and selected NMDP staff to establish telephone contact during times of high telephone line congestion and validate card accountability.
- NMDP Network Communication Drill was conducted using an NMDP proprietary tool; the drill involved sending an email to all Network Centers then tracks the time taken to respond by logging into the NMDP Network website.

o Continued to develop an NMDP Business Continuity Plan to improve the resiliency of the organization in the event of a catastrophic incident impacting the NMDP Coordinating Center.

o Continued to collect details for the Critical Document Registry which identified documents required to sustain operations immediately following a disaster. This involved identifying the documents as well as their location, be it physical or electronic.

o Provided business unit representation and business continuity expertise on the Steering Committee for the two-phase IT Disaster Recovery test conducted in April and May 2009.

o Continued to plan with IT staff to conduct a staff business continuity exercise tentatively scheduled for September where staff will perform key work duties from a remote work environment.

o Site visits were conducted at the NMDP operated donor centers in Charlotte, SC, Stanford, CA, and Oakland, CA.

- At these site visits the Business Continuity Planner reviews the Business Continuity Action Guide with staff to better prepare each location for responding to incidents that interrupt operations ranging from power or Internet outages to severe weather.

IIB. Rapid Identification of Matched Donors – Hypothesis 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1 Aim 1: Increase Registry Diversity	**Period 6 Activity:** **HLA** Five contracted laboratories performed HLA-A, B, DRB1 typing and one laboratory performed HLA-A, B, C, DRB1 typing, on 34,670 newly recruited donors funded by this grant. • Blind quality control testing error rate was 0.03%, meeting the project requirement of ≤ 2.0%. • On-time testing completion rate was 97%, meeting the project requirement of a minimum of 90% of typing results reported within 14 days of shipment of samples. During this period several HLA typing research projects were completed to refine allele frequency data and reagents and to increase the resolution and quality of HLA typing on the registry, especially from diverse donor populations. Specific alleles retested were: • The allele DRB1*0811 was described in March 1994 and is relatively common in NAM populations. Until reagents were added to type for DRB1*0811, samples would have been reported as DRB1*0802 or with codes that contain the DRB1*0802 allele. Samples with serologic typing at A and B were also retyped by DNA methods to upgrade the typing. Ninety three NAM samples were retyped and 33% of the donors' typings were corrected to reflect the new DRB1*0811 allele. • The allele DRB1*1506 was described in June 1996 and is seen in Asian populations. Until reagents were added to type for DRB1*1506, samples would have been reported as DRB1*1501 or with codes that contain DRB1*1501. It was postulated that Asian donors typed before January, 1997 may actually carry DRB1*1506. This cohort contained a relatively large number of samples. Rather than type all these samples, HapLogic was used to analyze the cohort and selectively remove samples with a low probability of carrying DRB1*1506. Samples with potential to type as DRB1*1506 and those where one or both haplotypes could not be predicted were retained for further typing (N=221).

Samples were also retyped at A and B by DNA methods to upgrade the typing.

Two hundred twenty one API samples were retyped. 85% of the initial DRB1*1501 results were found to be correct (187 of 221 results). However, when HLA-A and –B typing was repeated on this cohort, 7.2% and 11.3%, respectively, of the donor typings were found to be discrepant.

- Both of these projects highlight the importance of technical oversight of the Registry data and the necessity to carefully monitor the file in order to provide the most accurate HLA data for searching patients. The results of both analyses were submitted as abstracts to the 2009 ASHI annual meeting.

STAR II

- The STAR II transaction broker was released in May of 2009. Of note was a change to make the HML processor highly configurable with regard to the database versioning for lab typing kits. This will allow the NMDP to more quickly support new and different typing kits on a lab specific basis, and provides much more flexibility in accepting HLA information from labs for recipients and donors. In addition, this change provides flexibility for management of both operational (patient directed) and research-based lab results.

Adult Donor Registry

- To successfully serve all patients in need of cellular transplantation, the Marketing and Communications Department continued to focus on developing and executing strategies and tactics that help grow the Be The Match Registry^{SM} by increasing awareness, education and engagement among target audiences.
- During the April – June 2009 time-frame, we began developing strategies and tactics for the 2009-2010 Historical Black Colleges and Universities (HBCU) program. The program is an integrated marketing approach designed to build upon earlier work in this college segment to engage HBCU students, faculty, alumni and the broader HBCU community in our mission to save lives, specifically by joining the registry. The program will feature audience-specific awareness and educational tools, including a significant social media component to help ensure we reach students where they are today.

IIB.1 Aim 2: Evaluate HLA-DRB1 High Res typing	**Period 6 Activity:** • This task is closed.
IIB.1 Aim 3: Evaluate HLA-C Typing of Donors	**Period 6 Activity:** • This task is closed.
IIB.1 Aim 4: Evaluate Buccal Swabs	**Period 6 Activity:** • No activity this period.
IIB 1 Aim 5: Enhancing HLA Data for Selected Donors	**Period 6 Activity:** This aim consists of registry-based typing projects, which have the potential to strategically identify and improve the HLA typing and availability of donors most likely to match searching patients from domestic TCs. All strategies being evaluated are extensions of the previous Replacement Donor and Optimal Donor typing projects. • Back-Up Donor Project: While the primary study was completed in December 2007, the NMDP staff has continued to monitor the patient-directed utilization of the 206 donors prospectively typed in this project. To date we have observed the activation of 16 donors for CT requests, followed by 6 workup requests and 3 subsequent stem cell donations. An abstract reporting the results of this study was submitted to the 2009 ASHI annual meeting. • Optimal Donor Project: While the project was officially completed in 2008, NMDP staff has continued to monitor the patient-directed utilization of the 462 donors prospectively typed in this project. Current follow-up of these donors revealed the activation of 17 donors for CT requests, followed by 2 hold-for-workup requests, 2 workup requests and 1 stem cell donation. This demonstrates the ability of this project to selectively identify Registry donors that may be needed by future searching patients. An abstract reporting the results of this study was submitted to the 2009 ASHI annual meeting. • Preliminary Search / Donor Contact project (minority donor sub-group): prospective typing of 422 minority donors was completed in late October 2008. Current follow-up of these donors revealed the

activation of 2 donors for CT requests.

- **Evaluation of HLA-AB only typed donors potentially matching patients with formal searches**: Patient searches with active work-up requests were evaluated and searches identified for which there are relatively few 6/6 matched donors. The donors in the HLA-AB only type donor pool appearing on the search were evaluated for the opportunity find donors potentially matching the patient's phenotype. We have previously selected and typed 691 donors for HLA-DRB1, and have monitored the donors for patient-directed activation events. Prospective typing was completed in March 2009. Current follow-up of these donors revealed the activation of 4 donors for CT requests, and 1 workup request. We are currently designing reports to examine the potential to extend this prospective typing strategy to HLA-AB donors appearing on preliminary searches where there are relatively few 6/6 matched donors. This systematic strategy of identifying donors likely to match searching patients appears promising. Continued application and extension of this strategy may allow optimization of efforts to benefit future patients.
- **Continuing analysis of patients associated with Optimal Donor project that had zero potential 6/6 donor matches in NMDP hosted registry or BMDW**. We have approached this analysis from various perspectives to evaluate this patient group and the selection of HLA-AB only typed donors for prospective upgrade of their HLA typing.
  - A patient haplotype analysis has been run in an attempt to assess reasons for the difficult search; output data analysis is pending.
  - As previously reported, 4,931 donors were identified who potentially matched the study patients. Of these, 1,359 donors with repository samples were selected for prospective typing. AB only donors selected were associated with unique phenotypes not seen in the fully typed donor population or phenotypes with few (2-10) donors. Current follow-up of these donors revealed the activation of 8 donors for CT requests, followed by a stem cell donation for a patient who had searched for almost two years. These donors had been on the registry from 8-14.7 years prior to prospective typing, but were then activated for new patients within an average of 228 days.
  - Discussing other possible selection strategies for the next group of AB only typed donors.
  - An abstract reporting the results of this study was submitted for consideration for the 2009

	Annual ASHI meeting. • Performed additional donor selections for prospective HLA typing using our Optimal Donor selection strategies now for patient phenotypes with only 1-2 potentially matching donors. NMDP staff shipped approximately 460 donor samples for prospective HLA typing during this reporting period. NMDP staff continues to monitor the patient-directed utilization of all donors typed through the project.
IIB 1 Aim 6: Maintain a Quality Control Program	**Period 6 Activity:** • 80 new unique B-LCLs were added to the QC Master inventory. Blind QC Swab samples will be created from these cell lines for shipment as needed. • Sample Storage Research Study (SSRS) B-LCL samples were sent to two laboratories for the 18-month time point of the QC portion of the study. Preliminary review of the data shows 100% accuracy in HLA typing, and good quality and quantity of DNA for all swabs. This is the final time point for the QC portion of the SSRS.
IIB. Rapid Identification of Matched Donors – Hypothesis 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB 2 Aim 1: Collection of Primary Data	**Period 6 Activity:** • No activity this period.
IIB 2 Aim 2: Validation of Logic of Primary Data	**Period 6 Activity:** • This task is closed.
IIB 2 Aim 3: Reinterpretation of Primary Data	**Period 6 Activity:** • This task is closed.
IIB 2 Aim 4: Genotype Lists & Matching Algorithm	**Period 6 Activity:** • No activity this period.

IIB. Rapid Identification of Matched Donors – Hypothesis 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3 Aim 1: Phase I of EM Haplotype Logic	**Period 6 Activity:** • No activity to report for this period.
IIB 3 Aim 2: Enhancement of EM Algorithm	**Period 6 Activity:** • No activity this period.
IIB 3 Aim 3: Optimal Registry Size Analysis	**Period 6 Activity:** • No activity this period.
IIB 3 Aim 4: Target Under-represented Phenotypes	**Period 6 Activity:** • No activity this period.
IIB 3 Aim 5: Bioinformatics Web Site	**Period 6 Activity:** • This task is closed.
IIB 3 Aim 6: Consultants to Improve Algorithm	**Period 6 Activity:** Funding on this aim provides support for the SSA program provided to TCs to meet their need for HLA expertise for unrelated stem cell donor selection. The program includes external and internal HLA experts who review each patient search and write a report summarizing a search strategy to assist the TC in rapidly identifying the best potential stem cell source for their patient. The HLA experts provided valuable feedback for algorithm and IT enhancements throughout the quarter. The SSA program completed 384 patient reports for 78 TCs during this quarter. The average turnaround time for all reviews was 3.9 business days which met the program requirement of 5 business days.

IIB. Rapid Identification of Matched Donors – Hypothesis 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4 Aim 1: Expand Network Communications	**Period 6 Activity:** • No activity to report for this period.
IIB.4 Aim 2: Central Contingency Management	**Period 6 Activity:** • NMDP recently launched three online CME modules to educate referring physicians on the advances in unrelated transplantation. NMDP will produce companion fact sheets that will summarize key learning from the modules and also serve to generate interest in viewing the programs online.
IIB.4 Aim 2: Benchmarking Analysis	**Period 6 Activity:** • This task is closed.
IIB.4 Aim 2: Expand Capabilities of Collection and Apheresis Centers	**Period 6 Activity:** During Q3 of FY2009, Phase III of the strategic planning facilitated by LSSG was completed and a report was submitted to the NMDP core AC/CC team on May 28, 2009. Phase III consisted primarily of an Assessment and Tactical Recommendations for an NMDP Recognition Program, wherein the final strategy Phase IIa was researched by conducting network interviews and presented to the core AC/CC team with tactical recommendations for implementation. The core AC/CC team is currently working with the recommendations to develop a plan for recognition of participating apheresis and marrow collection centers. In addition to the Recognition program, a final plan for Standardization of Procedures of Interaction (POI) has been developed. A working team has been identified and work has begun in accordance with the plan, with the expectation of completion of a more standardized approach to POI to be ready by the September 30, 2009.

	Also in addition to the above mentioned plans, an AC / CC Tiering and Regionalization project plan is being developed, per the original core AC/CC team tactical planning. At this point, centers of interest have been identified as have criteria for determination of which centers have the most potential to meet the NMDP need for a tiered network model for collections. The plan for Regionalization will be formalized by January 1, 2010.
IIC. Immunogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1 Aim 1: Donor Recipient Pair Project	**Period 6 Activity:** In 1994 a retrospective Donor/Recipient Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. • Scientific Services staff compiled all outstanding typing issues from prior SGs and distributed samples to a tie-breaker laboratory for final resolution. All results were reported in June. Full analysis and audit will be completed early next quarter. • Sample Group 22 (SG22) period of performance came to a close on April 30, 2009. The contracts for SG22 (273 pairs) included intermediate and high resolution HLA typing. During the quarter, the discrepancy, no-make, and linkage analyses were initiated. • The project period for SG23 began April 30, 2009 and will come to a close on August 31, 2009. The contracts for SG23 (400 pairs) testing includes intermediate and high resolution HLA. Current HLA matching guidelines for unrelated HCT recommend avoidance of mismatches only within the antigen recognition site (ARS). This recommendation is based on the hypothesis that amino acid differences outside the ARS are not immunogenic. The ARS allo-reactivity assessment project will give insight into the allowable percent tolerance of matching needed outside of the ARS.

	• Initiated investigation of the first class II non-ARS mismatch (DRB1*140101/1454) where both alleles have been seen in the same genotype. Specific queries of the Be The Match Registry allowed for selection of ninety-nine potential donors to be typed at high resolution. Study participation selection will occur in the next quarter once typing results have been evaluated.
IIC. Immunogenetic Studies – Hypothesis 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC 2 Aim 1: Analysis of non-HLA loci	**Period 6 Activity:** In 2005 a pilot study to perform high resolution KIR gene typing was launched. The primary objectives of the study were to move technology forward from the current practice of locus level typing to high resolution typing, disseminate information and protocols in an open source mechanism and develop reference lines for use in individual laboratories. • Resolution continued of 128 potential new KIR alleles found within Phase 1, 2 and 3 of the KIR Typing Pilot. 78 samples were determined to have 46 novel alleles. Only two samples still remain to be typed. Submission, naming and publication should occur within the next two quarters. • Manuscript preparation for the KIR Typing Pilot Project continued. Further analysis of the data is ongoing. Presentation of the data will occur at the end of next quarter. • To date 1173 pairs from the Donor/Recipient pairs project have been typed for presence/absence of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1). The IPR database and its applications will allow for storage and analysis of all immunogenetic data collected on NMDP research samples. This database will replace the existing HLA donor/recipient pairs database and facilitate storage and analysis of data from other immunogenetic loci (KIR, microsatellites, single nucleotide polymorphisms, etc). • The Scientific Services and Bioinformatics departments continued to collaborate on the design and development of the IPR database application and tools. • The application that accepts, validates, and stores incoming HLA and KIR typing data via HML was completed and quality assurance testing will be completed early next quarter.

IIC 2 Aim 2: Related Pairs Research Repository	**Period 6 Activity:** Related transplant research sample collection continued with a pilot project initiated at seven TCs in December 2007. By the end of the reporting period, five TCs had submitted 567 samples (259 donor/recipient pairs) to the Repository. Development continues on the Research Sample Repository Tools suite to facilitate management of samples. Several enhancements were tested and released to production. The WGA project continued with the evaluation of the effectiveness of WGA using cord blood samples. In March of 2009 WGA was performed on 10 samples; five of which were of DNA extracted from cord blood and the other five of filter paper samples spotted with cord blood. All samples achieved amplification close to the expected amount of 40ug from an initial input of 10ng. • In order to validate the effectiveness and reliability of WGA at producing unbiased, high quantity and quality DNA products, the amplified DNA samples were high resolution typed at HLA- A, B, C, DRB1, DQB1, and DPB1 by SBT. • One cord filter paper sample resulted in a different set of typing results. A silent mutation was found in exon 3 codon 95 (ATC>ATT) for HLA-A. Testing of the original filter paper genomic DNA will be completed early next quarter to determine whether the silent mutation was inserted during the WGA process. **Evaluation of Cyto-Chex blood collection tubes as a method to obtain phenotypically stabilized cells for analysis.** Phenotypically stabilized cells would be a valuable tool for sample collection in support of clinical trials and for potential addition to the NMDP Research Repository inventory. • The preservative used in Cyto-Chex tubes has been shown to minimize the adverse effects that time, storage and transport conditions can have on sample integrity. Cell morphology and cellular antigen expression for many cell markers measured in HIV patients has been shown to be maintained for up to 7 days. These stabilized samples can be shipped and stored at ambient temperatures. • Three current BMT-CTN contract laboratories with expertise in phenotype analysis of T, B, NK and dendritic cell subsets are participating in the project. o **LAB A**: T, B, NK, and dendritic cell subset panels and intracellular Foxp3 staining. o **LAB B:** regulatory T-cells and intracellular Foxp3 staining.

	○ **LAB C**: activated B-cells • Peripheral blood was collected from laboratory volunteer donors. The Cyto-Chex tube collected samples were tested at baseline, 1, 3 and 7 days post-collection and compared to standard heparin tube collected samples. Testing results were received late this quarter and the final analysis will be reported next quarter. Preliminary review of the data indicated that the Cyto-Chex blood collection tubes did not efficiently stabilize many of the markers evaluated.
IID. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1 Aim 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 6 Activity:** **A Observational Research** • Staff continued work on various observational studies within the area of Immunobiology and GVHD and Graft Sources Working Committees. • A total of five manuscripts were published, and one submitted from the CIBMTR Working Committees supported under this grant during this reporting period. **Prospective Studies; RCI BMT** • Activity related to the BMT CTN PBSC vs. Marrow trial continued with a total of 532 donor/patient pairs randomized at the end of this reporting quarter. Accrual at the end of June was 97% complete. We anticipate completion of accrual to this study by the end of the next review period. Follow up activities will continue for two years on the patients and three years on the donors. • Adult Double Cord trial activity during this period included four patients being enrolled for a total of 16 patients accrued to this study, giving us a 29% completion rate. Staff continues to coordinate and complete monthly PI and coordinator calls, manage data collection and monitor sites. During this report period staff updated a variety of coordinator and site materials. • Revlemid trial activity continued to progress forward. An additional six sites were activated and open to accrual for a total of eight. During this reporting period three patients accrued for a total of four. The study was reviewed by the DSMB for its planned renewal and was approved to continue.

- Activity was completed on the protocol development for the AZA study titled *Low Intensity Therapy of MDS Prior to Non-Ablative Allogeneic Stem Cell Transplantation.* Additional funding continues to be explored to support portions of this study.

Work continued during this reporting period on building and testing of FormsNet platform for donor management. In addition staff worked to develop a requirements document for the FormsNet platform to support clinical trial management.

The Cord Blood Research sub-Committee met monthly to discuss study priorities and plan analyses. Activity during the past quarter focused on the following areas:

- A challenge grant application to the NHLBI to support a study to investigate biomarkers associated with cord blood engraftment was submitted. The study will evaluate a panel of assays on cord blood segments distributed for HLA confirmatory typing by the NMDP cord blood bank Network and correlate the results with engraftment data from the CIBMTR.
    - ONR support will assist with the validation of testing methods between the two laboratories during the project development phase starting early next quarter.
- Work continued on the data file preparation for an observational study of single versus double cord blood transplants in adults. The analysis will be completed early next quarter and an abstract submitted to the 2009 ASH meeting.
- The study design for a post thaw assessment of cord blood viability was submitted for consideration to the Research Subcommittee by PIs Allison Hubel and David McKenna. The subcommittee is working with the PIs to refine the study approach prior to approval.
- A study was developed to analyze the race and HLA matching of CBUs and recipients whose transplants were facilitated through the NMDP. The majority of CBUs distributed for racial minority recipients were not race matched. The best HLA matches were levels (6/6) were found in race matched pairs, except for African Americans. The results were submitted as an abstract to the 2009 ASHI annual meeting.
- The committee received a request from an assay manufacturer to consider acceptance of the results of a new assay system for the evaluation of CBUs.

	○ The Cord Committee decided to develop a white paper detailing recommendations/guidelines for the assessment of new assays (potency or other assays) relevant to cord blood banking and/or transplantation. A group of committee members, headed by the research subcommittee, has been assembled to be a part of the writing committee involved in the preparation of the white paper.
IID.1 Aim 2: Research with NMDP Donors	**Period 6 Activity:** • Staff continued support of a Donor Ethnicity study with Dr. Galen Switzer from the University of Pittsburgh. • Staff continued to collaborate on a COG KIR study. Activities include facilitating the collection of a donor blood sample and shipment to the study lab. To date, 21 patients have been enrolled and 67 donor sample requests have been facilitated. • Staff continued to develop a protocol for centralizing the NMDP long-term donor follow-up. The protocol is on track for approvals processes in fall 2009. • During this review period staff began to explore support of three additional studies.
IID.1 Aim 3: Expand Immuno-biology Research	**Period 6 Activity:** The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies • The committee focused considerable effort on the preparation of manuscripts describing the results of the various abstracts presented at ASH, BMT Tandem Meetings and EBMT in the past year. Several manuscripts will be submitted for publication next quarter. • The scientific director gave a plenary session talk on the impact of donor directed anti-HLA allo-antibodies in HLA mismatched stem cell transplantation at the 2009 Cord Blood Symposium in Los Angeles, California. • The scientific directors attended an NIH sponsored workshop on clinical trials endpoints for acute graft versus host disease after allogeneic stem cell transplantation in Rockville, Maryland. Funding for CIBMTR IBWC studies: • Research funds supported a prospective research sample collection protocol for a study of cGVHD in

	long-term surviving male recipients who received HSCT from female donors. Prospective blood samples were submitted by 24 of 28 consented participants. Sample analysis continues next quarter. • Research funds were requested to support DNA extraction and preparation of 408 samples for a study evaluating genome wide genetic diversity and the impact on acute graft versus host disease.

ACRONYM LIST

AABB	American Association of Blood Banks	IND	Investigational New Drug
AC	Apheresis Center	ICRHER	International Consortium for Research on Health Effects of Radiation
AFA	African American	IS	Information Services
AGNIS	A Growable Network Information System	IT	Information Technology
AML	Acute Myelogenous Leukemia	IRB	Institutional Review Board
API	Asian Pacific Islander	JCHO	Joint Commission of Healthcare Organizations
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	KIR	Killer Immunoglobulin-like Receptor
ASBMT	American Society for Blood and Marrow Transplantation	LSSG	Life Sciences Strategy Group
ASHI	American Society for Histocompatibility and Immunogenetics	MHC	Major Histocompatibility Complex
B-LCLs	B-Lymphocytic Cell Lines	MICA	MHC Class I-Like Molecule, Chain A
BARDA	Biomedical Advanced Research and Development Authority	MICB	MHC Class I-Like Molecule, Chain B
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MDACC	MD Anderson Cancer Center
BRT	Basic Radiation Training	MSKCC	Memorial Sloan-Kettering Cancer Center
CAU	Caucasian	MUD	Matched Unrelated Donor
C&A	Certification and Accreditation	NAM	Native American
CBMTG	Canadian Blood and Marrow Transplant Group	NCBM	National Conference of Black Mayors
CBB	Cord Blood Bank	NCI	National Cancer Institute
CBC	Congressional Black Caucus	NEMO	
CBS	Canadian Blood Service	NHLBI	National Heart Lung and Blood Institute
CBU	Cord Blood Unit	NIH	National Institutes of Health
CC	Collection Center	NIMS	National Incident Management System
CHTC	Certified Hematopoeitic Transplant Coordinator	NK	Natural Killer
CIBMTR	Center for International Blood & Marrow	NMDP	National Marrow Donor Program

	Transplant Research		
CLIA	Clinical Laboratory Improvement Amendment	NRP	National Response Plan
CME	Continuing Medical Education	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CMF	Community Matching Funds	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
COG	Children's Oncology Group	OIT	Office of Information Technology
CREG	Cross Reactive Groups	OMB	Office of Management and Budget
CSS	Center Support Services	ONR	Office of Naval Research
CT	Confirmatory Testing	P2P	Peer-to-Peer
CTA	Clinical Trial Application	PBMC	Peripheral Blood Mononuclear Cells
DC	Donor Center	PBSC	Peripheral Blood Stem Cell
DIY	Do it yourself	PCR	Polymerase Chain Reaction
DKMS	Deutsche Knochenmarkspenderdatei	PI	Principle Investigator
DMSO	Dimethylsulphoxide	POI	Procedures of Interaction
DNA	Deoxyribonucleic Acid	PSA	Public Service Announcement
D/R	Donor/Recipient	QC	Quality control
DSMB	Data Safety Monitoring Board	RCC	Renal Cell Carcinoma
EBMT	European Group for Blood and Marrow Transplantation	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
EM	Expectation Maximization	REAC/TS	Radiation Emergency Assistance Center/Training Site
EMDIS	European Marrow Donor Information System	RFP	Request for Proposal
ERSI	Environment Remote Sensing Institute	RFQ	Request for Quotation
FBI	Federal Bureau of Investigation	RG	Recruitment Group
FDA	Food and Drug Administration	RITN	Radiation Injury Treatment Network
FDR	Fund Drive Request	SBT	Sequence Based Typing
Fst	Fixation Index	SCTOD	Stem Cell Therapeutics Outcome Database
GETS	Government Emergency Telecommunications Service	SG	Sample Group
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SLW	STAR Link® Web

GIS	Geographic Information System	SSA	Search Strategy Advice
GvHD	Graft vs Host Disease	SSO	Sequence Specific Oligonucleotides
HBCU	Historical Black Colleges and University	SSP	Sequence Specific Primers
HCT	Hematopoietic Cell Transplantation	SSOP	Sequence Specific Oligonucleotide Probes
HHQ	Health History Questionnaire	SSRS	Sample Storage Research Study
HHS	Health and Human Services	STAR®	Search, Tracking and Registry
HIPAA	Health Insurance Portability and Accountability Act	TC	Transplant Center
HIV	Human Immunodeficiency Virus	TED	Transplant Essential Data
HLA	Human Leukocyte Antigen	TNC	Total Nucleated Cell
HML	Histoimmunogenetics Mark-up Language	TSA	Transportation Security Agency
HR	High Resolution	TTY	Text Telephone
HRSA	Health Resources and Services Administration	UI	User Interface
HSC	Hematopoietic Stem Cell	URD	Unrelated Donor
IBWC	Immunobiology Working Committee	WGA	Whole Genome Amplification
IDM	Infectious Disease Markers	WMDA	World Marrow Donor Association
IHWG	International Histocompatibility Working Group	WU	Work-up
IPR	Immunobiology Project Results		